

AMENDMENTS TO THE CLAIMS

The following listing of claims will replace all prior versions, and listings of claims in the application.

Claims 1 – 59 (Cancelled)

60. (Currently Amended) A grafted homodetic cyclopeptide combining both cell-targeting and therapeutic/diagnostic functions, obtained by the method as defined in claim 36 the cyclopeptide forming a framework that defines a grafted upper face and a grafted lower face; wherein one face is grafted with at least one molecule of therapeutic or diagnostic interest, and the other is grafted with at least one recognition molecule of interest; said cyclopeptide being obtained by a process comprising:

synthesizing a linear peptide from modified or unmodified amino acids, some of which carry orthogonal protective groups, whereby the linear peptide has a terminal glycine residue;

intramolecularly cyclizing the resulting protected linear peptide through the terminal glycine residue;

substituting some or all of orthogonal protective groups with a protected precursor suitable for grafting a molecule of interest; and

grafting at least one molecule of therapeutic or diagnostic interest on one face of the cyclopeptide framework, and at least one recognition molecule of interest on the other face of the cyclopeptide framework;

wherein at least one molecule of interest is grafted onto the upper or lower face of the framework via an oxime bond.

61. (Currently Amended) The grafted homodetic cyclopeptide as defined in claim 60, ~~grafted on one of its faces with~~ wherein at least one recognition molecule is a ligand of integrin $\alpha v \beta 3$ comprising peptides derived from ~~eyele(RGDfK)~~ cyclo(L-Arg-L-Gly-L-Asp-D-Phe-L-Lys) (SEQ ID NO: 1) and/or ~~eyele(RGDyK)~~ cyclo(L-Arg-L-Gly-L-Asp-D-Tyr-L-Lys) (SEQ ID NO: 2), which are ligands of integrin, and on the other of its faces with an KLAKKLAK (SEQ ID NO: 3) apoptogenic peptide, a known therapeutic doxorubicin molecule, or a protein that is toxic at the intracellular level.

62. (Currently Amended) The grafted homodetic cyclopeptide as defined in claim 60, ~~grafted on one of its faces with~~ wherein at least one recognition molecule is a ligand of integrin $\alpha v \beta 3$, comprising peptides derived from ~~eyele(RGDfK)~~ cyclo(L-Arg-L-Gly-L-Asp-D-Phe-L-Lys) (SEQ ID NO: 1) and/or ~~eyele(RGDyK)~~ cyclo(L-Arg-L-Gly-L-Asp-D-Tyr-L-Lys) (SEQ ID NO: 2), which are ligands of integrin, and grafted on the other of its faces with a detectable molecule of the chromophore, biotin, fluorophore, radioemitter type, or ~~a precursor~~ precursor thereof.

63. (Withdrawn/Currently Amended) The grafted homodetic cyclopeptide as defined in claim 60, wherein the recognition molecules grafted on one of its faces ~~with~~ are carbohydrate derivatives and the therapeutic molecules grafted on the other face ~~with~~ are one or several T-dependent epitopic peptides, one or several cytotoxic peptides, one or several therapeutic organic molecule(s), or a protein that is toxic at the intracellular level.

64. (Withdrawn/Currently Amended) The ~~graft~~ grafted homodetic cyclopeptide as defined in claim 60, wherein the recognition molecules grafted on one of its faces ~~with~~ are carbohydrate derivatives and the diagnostic molecules grafted on the other face of the framework ~~with~~ are one or several chromophore(s), one or several biotin(s), one or several fluorophore(s), one or several radioemitter(s), or a chemical precursor group or ligand.

65. (Withdrawn) The grafted homodetic cyclopeptide as defined in claim 60, grafted on one face with B-dependent epitopes of the carbohydrate type, or T-dependent epitopes, and an immunoadjuvant.

66. (Original) A therapeutic or diagnostic composition, comprising a grafted homodetic cyclopeptide as defined in claim 60.

67. (Withdrawn/Currently Amended) A method of treating cancer comprising administering to a patient in need thereof a therapeutically effective amount of a composition as defined in claim 66 ~~to a patient~~.

68. (Withdrawn) A method of treating cancer comprising administering a therapeutically effective amount of a composition as defined in claim 66 for the suppression of neoangiogenesis.

69. (New) A method for preparing a grafted homodetic cyclopeptide according to claim 60, comprising:

synthesizing a linear peptide from modified or unmodified amino acids, some of which carry orthogonal protective groups, whereby the linear peptide has a terminal glycine residue;

intramolecularly cyclizing the resulting protected linear peptide through the terminal glycine residue;

substituting some or all of orthogonal protective groups with a protected precursor suitable for grafting a molecule of interest; and

grafting at least one molecule of therapeutic or diagnostic interest on one face of the cyclopeptide framework, and at least one recognition molecule of interest on the other face of the cyclopeptide framework;

wherein at least one molecule of interest is grafted onto the upper or lower face of the framework via an oxime bond.

70. (New) The method as defined in claim 69, wherein synthesizing the linear peptide is performed on a solid phase, whereby the synthesis is initiated from a glycine residue whose carboxyl function is anchored to a resin, and wherein the step of cyclizing the resulting linear peptide is performed in solution after release of the peptide from the resin.

71. (New) The method as defined in claim 69, wherein synthesizing and cyclizing the linear peptide are performed entirely on solid phase.

72. (New) The method as defined in claim 71, wherein synthesizing the linear peptide is initiated with an amino acid residue whose side chain is anchored to a resin.

73. (New) The method as defined in claim 69, performed entirely or partially automated on a peptide-synthesizing robot.

74. (New) The method as defined in claim 69, wherein the cyclopeptide is formed from 5, 10 or 14 amino acid residues.

75. (New) The method as defined in claim 73, wherein the cyclopeptide has 10 or 14 amino acid residues and forms two turns, the two turns comprising an (L)Pro-(D)AA and/or (D)Pro-(L)AA combination, AA being an amino acid, the two turns being separated by three or five amino acid residues, respectively.

76. (New) The method as defined in claim 74, wherein the three or five amino acid residues each have, on a side chain, a chemical function initially protected orthogonally by a protective group, the protective groups being directed alternately to one side and the other of a median plane of the framework, and defining a lower and upper face with respect to that plane.

77. (New) The method as defined in claim 73, wherein the three or five amino acid residues are amino acid residues having an amine side chain.

78. (New) The method as defined in claim 73, wherein orthogonal protective groups of central amino acid residues are identical to one another, orthogonal protective groups of other amino acid residues are identical to one another, the orthogonal protective groups of the central amino acid residues, on the one hand, and the orthogonal protective groups of the other amino acid residues, on the other hand, are different from one another.

79. (New) The method as defined in claim 69, wherein grafting the framework is begun by substituting the orthogonal protective groups of the framework with a protected precursor of the oxyamine function or a protected masked precursor of the aldehyde function, or with a label.

80. (New) method as defined in claim 79, wherein the protected precursor is protected 2-oxyaminoacetic acid (OAA).

81. (New) The method as defined in claim 79, wherein the protected masked precursor is a serine residue, the amine and hydroxyl functions of which are protected, and oxidation of which releases an aldehyde group.

82. (New) The method as defined in claim 79, wherein the protected precursor is a precursor of the thiol function.

83. (New) The method as defined in claim 79, further comprising: substituting the orthogonal protective groups of the lower face of the framework with a label, and substituting orthogonal protective groups of the upper face of the framework with a protected precursor of the oxyamine function or of the aldehyde function.

84. (New) The method as defined in claim 79, further comprising: substituting the orthogonal protective groups of the lower face of the framework with a protected precursor of the oxyamine function, and substituting the orthogonal protective groups of the upper face of the framework with a protected masked precursor of the aldehyde function.

85. (New) The method as defined in claim 79, further comprising: substituting the orthogonal protective groups of the upper face of the framework with a protected precursor of the oxyamine function, and substituting the orthogonal protective groups of the lower face of the framework with a protected masked precursor of the aldehyde function.

86. (New) The method as defined in claim 79, wherein the oxyamine or aldehyde functions generated from the precursors, previously deprotected, are reacted with one or several molecules of interest or with an intermediate molecule carrying an aldehyde or oxyamine function, respectively.

87. (New) The method as defined in claim 86, wherein the molecules of interest are identical to or different from one another.

88. (New) The method as defined in claim 86, wherein the molecules of interest are selected from the group consisting of nucleic acids, peptides, oligosaccharides, or organic molecules.

89. (New) The method as defined in claim 88, wherein at least one of the molecules of interest is the cyclopentapeptide cyclo(L-Arg-L-Gly-L-Asp-D-Phe-L-Lys) (SEQ ID NO: 1).

90. (New) The method as defined in claim 88, wherein the oxyamine function of the precursor located on the framework is reacted with at least one molecule of interest carrying an aldehyde function, and the precursor of the aldehyde function located on the framework is oxidized and the reaction is continued by bringing the framework into contact with a molecule of interest or an intermediate molecule carrying an oxyamine function.

91. (New) The method as defined in claim 86, wherein the intermediate molecule carries an oxyamine function capable of reacting with the aldehyde function(s) located on the framework, and alternately carries a precursor of at least one aldehyde function.

92. (New) The method as defined in claim 71, performed entirely or partially automated on a peptide-synthesizing robot.